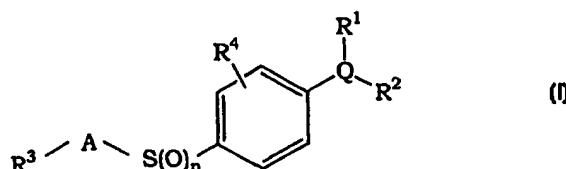




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : C07D 231/16, 231/14, 231/12, A61K 31/415, A61P 29/00		A3	(11) International Publication Number: WO 00/18741 (43) International Publication Date: 6 April 2000 (06.04.00)
(21) International Application Number: PCT/JP99/05289		(81) Designated States: BR, CA, CN, JP, KR, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).	
(22) International Filing Date: 27 September 1999 (27.09.99)			
(30) Priority Data: PP 6231 30 September 1998 (30.09.98) AU PQ 2243 16 August 1999 (16.08.99) AU		Published <i>With international search report.</i>	
(71) Applicant (for all designated States except US): FUJI-SAWA PHARMACEUTICAL CO., LTD. [JP/JP]; 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP).		(88) Date of publication of the international search report: 8 June 2000 (08.06.00)	
(72) Inventors; and			
(75) Inventors/Applicants (for US only): KONISHI, Nobukiyo [JP/JP]; 22-7, Aotanai, Nagaokakyo-shi, Kyoto 617-0811 (JP). NAKAMURA, Katsuya [JP/JP]; 12-1-103, Kamihamuro 2-chome, Takatsuki-shi, Osaka 569-1044 (JP). YAMAMOTO, Hirofumi [JP/JP]; 1-4-22-207, Kashio, Takarazuka-shi, Hyogo 665-0054 (JP). MANABE, Takashi [JP/JP]; 1-2-103, Maruyamadai, Kawanishi-shi, Hyogo 666-0152 (JP).			
(74) Agent: TAKASHIMA, Hajime; Yuki Building, 3-9, Hiranomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-0046 (JP).			

(54) Title: PYRAZOLE COMPOUNDS AS COX-2 INHIBITORS



(57) Abstract

A compound of formula (I), wherein R¹ is halo(lower)alkyl, halogen or cyano, R² is aryl optionally substituted with substituent(s) selected from the group consisting of halogen, lower alkoxy, cyano, nitro, lower alkenyl, amino, acyl and hydroxymino, R³ is hydrogen, lower hydroxy, acyloxy, lower alkoxy optionally substituted with lower alkoxy, amino optionally substituted with hydroxy or lower alkyl, lower alkylthio, or lower alkylsulfonyl, R⁴ is hydrogen or halogen, Q is pyrazolyl, A is lower alkylene optionally substituted with oxo or hydroxy, and n is 0, 1 or 2, provided that when R³ is hydrogen, R² is aryl substituted with lower alkenyl or A is lower alkylene substituted with oxo, or its salt, processes for their preparation and pharmaceutical compositions.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

INTERNATIONAL SEARCH REPORT

International Application No
PCT/JP 99/05289A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D231/16 C07D231/14 C07D231/12 A61K31/415 A61P29/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 13755 A (FUJISAWA PHARMACEUTICAL CO ; MATSUO MASAAKI (JP); OKUMURA KAZUO (JP) 17 April 1997 (1997-04-17) claim 1	2-12
A	TSUJI ET AL: "Studies on anti- inflammatory agents. V. Synthesis and pharmacological properties of 3-(difluoromethyl)-1-(4-methoxyphenyl)- 5-'4-(methylsulfinyl)phenyl!pyrazole and related compounds" CHEMICAL AND PHARMACEUTICAL BULLETIN, JP, PHARMACEUTICAL SOCIETY OF JAPAN, TOKYO, vol. 45, no. 9, September 1997 (1997-09), pages 1475-1481, XP002112607 ISSN: 0009-2363	2-12

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the International filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the International filing date but later than the priority date claimed

"T" later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the Invention

"X" document of particular relevance; the claimed Invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed Invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"a" document member of the same patent family

Date of the actual completion of the International search

15 March 2000

Date of mailing of the International search report

24/03/2000

Name and mailing address of the ISA
European Patent Office, P.B. 5018 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl
Fax: (+31-70) 340-3016

Authorized officer

De Jong, B

INTERNATIONAL SEARCH REPORT

Int'l Application No
PCT/JP 99/05289

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>TSUJI ET AL: "Studies on anti-inflammatory agents. IV. Synthesis and pharmacological properties of 1,5-diarylpyrazoles and related derivatives"</p> <p>CHEMICAL AND PHARMACEUTICAL BULLETIN, JP, PHARMACEUTICAL SOCIETY OF JAPAN, TOKYO, vol. 45, no. 6, June 1997 (1997-06), pages 987-995, XP002112608</p> <p>ISSN: 0009-2363</p>	2-12
A	<p>US 5 486 534 A (LEE LEN F ET AL)</p> <p>23 January 1996 (1996-01-23)</p>	2-12

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP 99/05289

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims No.: 10 because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claim 10 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compounds.

2. Claims No.: 1 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. Claims No.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims No.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims No.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1

Present claim 1 relates to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds according to claim 2.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int'l. and Application No

PCT/JP 99/05289

Patent document cited in search report	Publication date	Patent family member(s)			Publication date
WO 9713755	A 17-04-1997	AU	7146196	A	30-04-1997
		CA	2234511	A	17-04-1997
		CN	1203589	A	30-12-1998
		EP	0856000	A	05-08-1998
		JP	11513403	T	16-11-1999
US 5486534	A 23-01-1996	AU	3126795	A	22-02-1996
		CA	2195123	A	08-02-1996
		EP	0772597	A	14-05-1997
		JP	10503201	T	24-03-1998
		WO	9603385	A	08-02-1996
		US	5580985	A	03-12-1996
		US	5756530	A	26-05-1998